DCM who were treated with ICDs were enrolled in this study. Their left ventricular ejection fraction (LVEF) was 25±9%. During a regular followup period of up to 60 months (median 21 months), these patients received frequent appropriate (34%) and inappropriate (36%) ICD therapies. The first appropriate ICD therapy occurred at 7 months (median). Approximately 2/3 of these ICD therapies occurred within one year after implantation. There was no significant difference between patients on (n=81) and off ACE inhibitors in age (51±16 vs 52±15 years, p>0.05), LVEF (25.5±8.8% vs 23.2±9.2%, p>0.05), or incidence of documented spontaneous or inducible sustained ventricular tachycardia / fibrillation before implantation (36% vs 48%, p>0.05). Fewer patients on ACE inhibitors were treated with amiodarone (21% vs 48%, p<0.05). After adjustment of age, gender, LVEF, use of antiarrhythmic drugs, and incidence of pre-implant documented spontaneous or inducible sustained ventricular arrhythmias, the incidence of appropriate ICD therapy was significantly lower in patients on ACE inhibitors than those off ACE inhibitors (log rank p<0.05). At one year after implantation, ACE inhibitor therapy was associated with an 80% reduction in appropriate ICD therapy in these patients (18% vs 33%, log rank p<0.05).
Conclusion: ACE inhibitor therapy may substantially reduce the incidence of appropriate ICD therapy in patients with CHF secondary to idiopathic DCM. These observations suggest that ACE inhibitors may have important direct and/or indirect antiarrhythmic actions.

3:00 p.m.

817-5 Implant Defibrillator Threshold Characteristics in an Implantable Cardioverter Defibrillator Population Receiving Cardiac Resynchronization Therapy

Claudio Schuger, Kenneth Ellenbogen, Mitchell Faddis, Bradley P. Knight, Patrick Yong, Ross Sample, The VENTAK CHF/CONTAK CD Study Investigators, Henry Ford Hospital, Detroit, MI, Guidant Corporation, St. Paul, MN

Background: Common practice during implantable cardioverter defibrillator (ICD) implant is to perform defibrillation threshold (DFT) testing by converting induced ventricular fibrillation (VF) with a minimum 10-joule (J) safety margin. Patients (pts) with severe left ventricular dysfunction may require additional energy to terminate VF and predicting who is at risk for elevated DFTs would be of benefit.
Methods: Pts requiring ICD therapy, a history of congestive heart failure (NYHA Class II-IV) and QRS >=120 ms were enrolled in the CONTAK CD study and received cardiac resynchronization devices with ICD capability. The protocol recommended one of two methods of DFT: either VF conversion testing with at least two successful conversions <= 21J or step down DFT testing. Multivariate logistic regression was performed to determine factors predictive of DFT test outcome.
Results: Of 501 pts enrolled, DFT recommendations were met in 444 (88.6%), with VF conversion testing performed in 396 (79.0%) and step down DFT testing in 48 (9.6%) with mean DFT of 10.7±4.6 J. DFT recommendations were not met in 57 pts (11.4%). Of these, 31 pts (6.2%) had converted with energies >= 23J or had no DFT testing performed due to pt condition and received a device without meeting implant recommendations. The remaining 26 pts (5.2%) began DFT testing, but terminated testing prematurely due to pt condition. In the 31 pts with elevated or untested DFT, larger left ventricular internal dimension in diastole (LVIDd) (p=0.003) and prolonged procedure time (p=0.01) were significant predictors of higher energy requirements. Subcutaneous arrays were used in nine pts (1.8%). Six met implant recommendations with its use, one did not, and two pts were not tested.
Conclusion: DFT testing with adequate safety margin is accomplished successfully in the majority of this high-risk ICD pt population. However, in a significant number of pts, a 10J safety margin cannot be ascertained. LVIDd and prolonged procedure time may predict higher DFT and could be used to anticipate the need for alternative shocking vectors (such as subcutaneous array or patch electrode) or assuring the availability of a high-energy device.

3:15 p.m.

817-6 Delineation of the Pericardiophrenic Vein for Optimal Left Ventricular Lead Placement

Marmar Vaseghi, David Cesario, Sen Ji, Kevin Shannon, Isaac Wiener, Gregg Fonarow, Jonah Odim, Miguel Valderrabano, Kalyanam Shivkumar, UCLA Cardiac Arrhythmia Center, Los Angeles, CA

Background: Biventricular pacing has established benefits for the management of drug refractory heart failure. However, optimal placement of the left ventricular (LV) lead can occasionally be associated with left phrenic nerve stimulation. The purpose of this study was to define the value of identifying the pericardiophrenic vein, by venography or direct visualization, for optimal LV lead placement. The pericardiophrenic vein runs along with the left phrenic nerve and serves as a radiographic marker for sites with likely phrenic nerve stimulation during LV lead placement. **Methods:** We analyzed data from 84 patients who underwent biventricular device implantation between July 2002 and September 2003. Eighty transvenous implants, one LV endocardial implant, and three surgical epicardial implants (including one previously failed transvenous implant) were performed. Sixty five patients (77%) had ischemic cardiomyopathy. **Results:** In four patients the pericardiophrenic vein was identified either during occlusion venography of the CS (post thoracotomy, veno-venous collaterals, n=1) or during selective cannulation of the pericardiophrenic vein (using a DAIG Csl catheter, n=3). The vein was directly visualized in three patients who underwent surgical LV lead implantation. Whether placed in the coronary veins or on the epicardium, LV leads in these cases were implanted in areas not overlying the pre-identified pericardiophrenic vein. During follow-up, none of the patients who had LV leads placed with prior delineation of the pericardiophrenic vein had any evidence of phrenic nerve stimulation. However, three patients (4%) in whom the pericardiophrenic vein was not identified developed phrenic nerve stimulation. **Conclusions:** Identification of the pericardiophrenic vein is feasible in all patients undergoing surgical LV lead placement, and with the aide of angiography, in selected patients undergoing transvenous LV lead implantation. Phrenic nerve stimulation by the LV leads can be avoided by placement of the leads away from the previously identified pericardiophrenic vein, reducing the incidence of phrenic nerve stimulation.

POSTER SESSION

1110

Mechanisms of Arrhythmias: From Cells to the In Situ Heart

Monday, March 08, 2004, 3:00 p.m.-5:00 p.m.
Morial Convention Center, Hall G
Presentation Hour: 4:00 p.m.-5:00 p.m.

1110-213 Ranolazine Attenuates Increased Variability of Action Potential Duration and After Depolarizations Caused by Augmentation of Late Sodium Current

Yejia Song, Lin Wu, John C. Shryock, Luiz Belardinelli, University of Florida, Gainesville, FL, CV Therapeutics, Palo Alto, CA

Background: This study assessed the hypothesis that an increase of late sodium current ($I_{Na(L)}$) exacerbates beat-to-beat variability of action potential duration (APD) and facilitates the actions of potassium-channel blockers to induce early afterdepolarizations (EADs).
Methods: $I_{Na(L)}$ and action potentials (APs) of guinea pig isolated ventricular myocytes were measured using whole-cell patch-clamp techniques.
Results: The $I_{Na(L)}$ enhancer ATX-II (5 nmol/L) increased the amplitude of $I_{Na(L)}$ by 217±39 pA (n=9, p<0.001). ATX-II (15 nmol/L) prolonged the APD measured at 50% repolarization (APD_{50}) by 244±24% from 281±11 to 963±61 ms (n=7, p<0.001) and induced EADs. Moreover, ATX-II increased the variability of APD_{50} (SD/mean of 10 consecutive APs, x100) from 1.1±0.3 to 16.2±0.7% (n=7, p<0.001). Ranolazine (10 μmol/L), an anti-ischemic agent and a putative inhibitor of $I_{Na(L)}$, attenuated the ATX-II-induced $I_{Na(L)}$ by 37±3% (p<0.05). The inhibition by ranolazine of $I_{Na(L)}$ was mimicked by tetrodotoxin (10 μmol/L, n=5). In the presence of ATX-II, Ranolazine (10 μmol/L) shortened the APD_{50} to 378±34 ms (p<0.001), abolished the EADs, and reduced the variability of APD_{50} to 2.8±0.4% (p<0.001). Although ATX-II at a low concentration (3 nmol/L) increased the APD_{50} by only 6±2% (n=11), it facilitated the actions of E-4031 (1 μmol/L) and chromanol 293B (30 μmol/L), blockers of the rapid and slow components of the delayed rectifier potassium current, respectively, to prolong the APD_{50}. In the absence and presence of ATX-II, the APD_{50} was increased by 11±2% (n=6) and 104±41% (n=8) by E-4031 (p<0.01), and 40±7% (n=6) and 202±59% (n=9) by 293B (p<0.001), respectively. EADs were induced by E-4031 and 293B only in the presence of ATX-II. Ranolazine (10 μmol/L) abolished the EADs and reversed the prolongation of APD_{50} by 76±5% (n=5, p<0.01) and 71±4% (n=9, p<0.001), respectively, in the presence of ATX-II plus E-4031 or 293B.
Conclusion: An augmentation of $I_{Na(L)}$ greatly increased the variability of APD and facilitated the proarrhythmic effects of potassium-channel blockers. Inhibition of $I_{Na(L)}$, such as by ranolazine, may reverse dispersion of repolarization, drug-induced QT prolongation, and arrhythmias.

1110-214 Ischemia/Reperfusion Induced Intracellular Calcium Oscillations in the Intact Heart: Relation to Arrhythmogenesis

Vikram Lakireddy, Paramdeep Baweja, Gil Bub, Tamara Baynham, Nabil El-Sherif, Downstate Medical Center, Brooklyn, NY, VA New York Harbor Health Care System, Brooklyn, NY

Background: Intracellular calcium (iCa) loading by various mechanisms, including ischemia /reperfusion (I/R), has been postulated to cause spontaneous oscillatory Ca^{2+} release from the sarcoplasmic reticulum that may play a role in generation of arrythmia. Thus far, this mechanism has been demonstrated in isolated cardiomyocytes or 2-dimensional myocyte networks. We investigated the development of iCa oscillations (O) during I/R in the intact heart.
Methods: Perfused Langendorff guinea pig hearts were subjected to global I/R (20 min./ 20 min.). The heart was stained with 100 microliters of Rhod-2 AM and 25 microliters of RH-327. Membrane voltage (Vm) and iCa were simultaneously recorded with an optical mapping system of two 16x16 photodiode arrays. Activation maps of both Vm and iCa were constructed.
Results: O at varying cycle lengths (200-600ms) were observed to develop at well localized focal sites within the mapped surface where iCa signal preceded Vm signal by 10-20ms. O that followed the iCa transient of a basic beat manifested in the Vm as early afterdepolarizations. Intermittent conduction from the focal site of O to the rest of the heart manifested as occasional premature beats , trigeminal, or bigeminal rhythm. A regular conduction pattern from a focal site of fast O manifested as regular tachycardia of focal origin. A complex conduction pattern of fast O resulted in wavebreaks and induction of ventricular fibrillation (VF).
Conclusion: We have shown, for the first time, the development of focal O during I/R in the intact heart. Depending on the conduction pattern, O can result in a single premature beat or regular tachycardia, or can induce VF. In the setting of I/R, an occasional premature beat may represent the “tip of the iceberg” of an underlying potentially serious arrythmogenic mechanism.